

Optimizing Isoprenoid Biosynthesis

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Isoprenoids are a diverse class of natural compounds that hold great commercial potential. The mevalonate pathway is one of the major pathways for isoprenoids biosynthesis. In the keasling lab, mevalonate pathway has been divided into two operons: the top pathway, and the lower pathway. We have shown that the lower mevalonate pathway is the limiting part of the mevalonate pathway and needs further optimization. We have shown that mevalonate kinase which is the first gene of the lower pathway is limiting. We are studying the kinetics of mevalonate kinase to determine the cause of this limitation. Also we are trying different ribosome binding sites with different strengths in front of the genes in the lower mevalonate pathway to optimize protein expression and therefore reach optimal metabolite production. For this purpose, it is desired to be able to measure pathway intermediates to determine which steps of the pathway are limiting, causing the intermediate metabolites to accumulate. We are trying to understand how the pathway expression is regulated when certain toxic intermediates accumulate. We hope that this work would help us in further optimizing the isoprenoids biosynthetic pathway and constructing new pathways.